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Facsimile Cover

Date: February 17, 2004

TO	**Examiner Marschel**		
Fax Number.	**703 872 9306**	Company:	USPTO
Telephone:	571 272 0718	Your Reference:	SN 10/608,092
FROM:	**Malcolm K. McGowan, Ph.D.**		
Telephone:	703.838.6630	Our Reference:	028723-384
Sent By:	Sally Dankers	Number of Pages Including Cover:	31

Message

Attached is Request for Interference, Transmittal and fax confirmation sheet originally filed September 9, 2003, retransmitted today per telephonic request of Examiner Marschel at 571 272 0718.

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****************** -COMM. * VAL- ******************* DATE SEP-09-2003 ** TIME 15:49 *** P.01

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Fax Tel. No.:	703 746 4991	Sent By:	Sally Dankers
Your Ref.:	10/608,092	Our Ref.:	028723-384
		Total Pages (Incl. Cover Page):	30

RE: Request by Applicants for Interference Pursuant to 37 C.F.R. § 1.607

MESSAGE:

Patent
Attorney's Docket No. 028723-384

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

JOE W. GRAY et al.

Application No.: 10/608,092

Filed: June 30, 2003

For: CHROMOSOME-SPECIFIC STAINING TO DETECT GENETIC REARRANGEMENTS

Group Art Unit: 1655

Examiner: A. Marschel

Confirmation No.:

REPLY TRANSMITTAL LETTER

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Enclosed is a **Request by Applicants for Interference Pursuant to 37 CFR 1.607** for the above-identified patent application.

[ ] A Petition for Extension of Time is also enclosed.

[ ] A Terminal Disclaimer and the [ ] $55.00 (2814) [ ] $110.00 (1814) fee due under 37 C.F.R. § 1.20(d) are also enclosed.

[ ] Also enclosed is/are _____.

[ ] Small entity status is hereby claimed.

[ ] Applicant(s) requests continued examination under 37 C.F.R. § 1.114 and enclose the [ ] $375.00 (2801) [ ] $750.00 (1801) fee due under 37 C.F.R. § 1.17(e).

[ ] Applicant(s) requests that any previously unentered after final amendments not be entered. Continued examination is requested based on the enclosed documents identified above.

[ ] Applicant(s) previously submitted ___, on ___, for which continued examination is requested.

[ ] Applicant(s) requests suspension of action by the Office until at least ___, which does not exceed three months from the filing of this RCE, in accordance with 37 C.F.R. § 1.103(c). The required fee under 37 C.F.R. § 1.17(i) is enclosed.

DOCKETED (703) CSH
filed 9.9.03 BY

[ ] A Request for Entry and Consideration of Submission under 37 C.F.R. § 1.129(a) (1809/2809) is also enclosed.

[X] No additional claim fee is required.

[ ] An additional claim fee is required, and is calculated as shown below:

AMENDED CLAIMS					
	NO. OF CLAIMS	HIGHEST NO. OF CLAIMS PREVIOUSLY PAID FOR	EXTRA CLAIMS	RATE	ADD'L FEE
Total Claims		MINUS =		× $18.00 (1202) =	
Independent Claims		MINUS =		× $84.00 (1201) =	
If Amendment adds multiple dependent claims, add $280.00 (1203)					
Total Claim Amendment Fee					
If small entity status is claimed, subtract 50% of Total Claim Amendment Fee					
TOTAL ADDITIONAL CLAIM FEE DUE FOR THIS AMENDMENT					

[ ] A total fee in the amount of $ _____ is enclosed.

[ ] Charge $_____ to Deposit Account No. 02-4800.

The Director is hereby authorized to charge any appropriate fees under 37 C.F.R. §§ 1.16, 1.17, 1.20(d) and 1.21 that may be required by this paper, and to credit any overpayment, to Deposit Account No. 02-4800. This paper is submitted in duplicate.

Respectfully submitted,

BURNS, DOANE, SWECKER & MATHIS, L.L.P.

Date: September 9, 2003

By: _____
Malcolm K. McGowan, Ph.D.
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(05/03)

Patent
Attorney Docket No. 028723-384

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of

JOE W. GRAY et al

Application No.: 10/608,092 Group Art Unit: 1655

Filed: June 30, 2003 Examiner: A. Marschel

For: A METHOD OF DETECTING GENETIC TRANSCLOCATIONS IDENTIFIED WITH CHROMOSOMAL ABNORMALITIES

REQUEST BY APPLICANTS FOR INTERFERENCE PURSUANT TO 37 CFR 1.607

Honorable Commissioner of Patents and Trademarks
Washington, D.C. 20231

Sir:

Applicants respectfully request that an interference be declared between the application identified in caption and U.S. Patent No. 6,414,133[1] ("the '133 patent"). Applicants respectfully point out that examination of the present application should "be conducted with special dispatch" because it requests an interference with an issued patent. 37 CFR 1.607(b); MPEP 708.01 and 2307.

As explained in detail below, Applicants request that the interference be declared:

(i) Employing the proposed Count set forth in attached Appendix A;

(ii) With claims 1-3, 5-12, and 14-19 of the '133 patent and claims 127-143 of the present application designated as corresponding to the Proposed Count; and

[1] The '133 patent was submitted in the IDS filed on 26 August 2003.

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(iii) Applicants indicated to be entitled to the benefit of application Serial No. 07/537,305 filed June 12, 1990[2].

Further, upon a determination by the Examiner that an interference should be declared, immediate issuance of a Notice suspending prosecution pending declaration of an interference is respectfully requested.

In support of the Request for Interference, Applicants present below sections (1)-(6) corresponding to the sections of 37 CFR 1.607.

(1) Identifying the patent

The patent against which Applicants request an interference is U.S. Patent No. 6,414,133 which lists as inventors Jeanne Dietz-Band, Wang-Ting Hsieh, and John F. Connaughton. The patent issued July 2, 2002, and is assigned on its face to Ventana Medical Systems, Inc. The patent was issued on application Serial No. 09/170,630, filed October 13, 1998. Because the instant application claims priority from application Serial No. 07/537,305, filed June 12, 1990, the present Applicants should be designated Senior Party, and Dietz-Band et al. should be designated Junior Party.

(2) Presentation of a proposed Count

Applicants propose a Count as follows:

A DNA probe set, said probe set comprising a first probe set and a second probe set,

[2] The present application is a divisional of application Serial No. 08/487,974, filed June 7, 1995, which is a continuation of 08/342,028, filed November 16, 1994 (now abandoned), which is a continuation of application Serial No. 08/181,367, filed January 14, 1994 (now abandoned), which is a continuation of application Serial No. 08/054,353, filed April 28, 1993 (abandoned), which is a continuation of application Serial No. 07/537,305, filed June 12, 1990. While the application previously claimed the benefit of earlier applications, the priority claim has been amended to reflect the proper priority claim for the claims pending in the present application.

said first probe set being sufficient in length and substantially complementary to an entire breakpoint region of a first DNA and nucleotides on both sides of the breakpoint region but less than an entire chromosome such that said first probe set will hybridize to both sides of the breakpoint region regardless of whether the first DNA has been broken in the breakpoint region and either end fused to another DNA, and

said second probe set being sufficient in length and substantially complementary to an entire breakpoint region of a second DNA and nucleotides on both sides of the breakpoint region but less than an entire chromosome such that said second probe set will hybridize to both sides of the breakpoint region regardless of whether the second DNA has been broken in the breakpoint region and either end fused to another DNA;

wherein said probes are detectably labeled; and

wherein said first DNA is part of the ABL1 gene on chromosome 9 and the second DNA is part of the BCR gene on chromosome 22.

The proposed Count is also presented in Appendix A.

Applicants note, pursuant to 37 CFR 1.606, that the proposed Count is identical to claim 3 of the '133 patent, written in independent form, and to claim 129 of the present application, written in independent form.

(3) Identification of claims in the '133 patent corresponding to the proposed Count

According to 37 CFR 1.606, "[a]ll claims in the application and patent which define the same patentable invention as a count shall be designated to correspond to the count." "Same patentable invention" is defined by 37 CFR 1.601(n), which states

> (n) Invention "A" is the *same patentable invention* as invention "B" when invention "A" is the same as (35 U.S.C. 102) or is obvious (35 U.S.C. 103) in view of invention "B" assuming invention "B" is prior art with respect to invention "A". Invention "A" is a *separate patentable invention* with respect to invention "B" when invention "A" is new (35 U.S.C. 102) and non-obvious (35 U.S.C. 103) in view of invention "B" assuming invention "B" is prior art with respect to invention "A".

Claims 1-3, 5-12, and 14-19 of the '133 patent, correspond to the proposed Count.

Claim 3

The proposed Count is identical to claim 3 of the '133 patent.

Claim 2

Claim 2 is directed to the probe set of claim 1, wherein the probes are detectably labeled. Claim 2 defines a genus from which claim 3 depends. Consequently, if claim 3 were prior art to Claim 2, it would anticipate claim 2. *In re Slayter*, 275 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960)("A generic claim cannot be allowed to applicant if the prior art discloses a species falling within the claimed genus."); *In re Gosteli*, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989). In addition, Dietz-Band admits, at col 9, lines 4-32 of the '133 patent, that detectable labels for probes, and methods of labeling probes, are known in the art. Claim 2 is thus directed to the same patentable invention as claim 3 and the Count, and so corresponds to the proposed Count.

Claim 1

Likewise, as claim 2 depends from claim 1, claim 3 is a species of the genus defined by claim 1. Consequently, if claim 3 were prior art to claim 1, it would anticipate claim 1. Claim 1 is thus directed to the same patentable invention as claim 3 and the Count, and so corresponds to the proposed Count.

Claim 5

Claim 5 is directed to a kit comprising a probe set according to claim 1. Kits are conventional in the art. For example, the 1988 Stratagene Catalog, at p. 39 (Appendix C), motivates and suggests that the assemblage of materials into kits which may be pre-mixed for the benefits therein cited such as availability and quality testing etc. Kits are also well known in biochemical work with either individual or mixed components ready for use. Thus it would have

been obvious to one of ordinary skill in the art at the time of the filing of the '133 patent, in possession of the probe set of claim 1, to assemble the components of that probe set into a kit as suggested by the Stratagene Catalog. As claim 5 is obvious over claim 1, it is likewise obvious over claim 3 and the proposed Count for the reasons discussed above in connection with claim 1.

Claim 6

Claim 6 is directed to a diagnostic kit according to claim 5, comprising at least two containers, each of which contains a reagent comprising a probe set according to claim 1. Claim 6 is obvious over claims 5, 1, and 3, and the proposed Count, for the reasons discussed in connection with claim 5, above.

Claim 7

Claim 7 is directed to a diagnostic kit according to claim 6, wherein the recited reagent contains both the first and second probe set according to claim 1. Claim 7 is obvious over claim 3 and the proposed Count, for the reasons discussed in connection with claims 5 and 6 above.

Claim 8

Claim 8 is worded similarly to claim 1. A side-by-side comparison of claims 1 and 8 is shown below.

1. A DNA probe set, said probe set comprising a first probe set and a second probe set,	8. A DNA probe set, said probe set comprising a first probe set and a second probe set,
said first probe set being sufficient in length and substantially complementary to an entire breakpoint region of a first DNA and	said first probe set being sufficient in length and substantially complementary to an entire breakpoint region of a first DNA and

nucleotides on both sides of the breakpoint region but less than an entire chromosome such that said first probe set will hybridize to both sides of the breakpoint region regardless of whether **the first DNA has been broken in the breakpoint region and either end fused to another DNA, and**	nucleotides on both sides of the breakpoint region but less than an entire chromosome such that said first probe set will hybridize to both sides of the breakpoint region regardless of whether **a second DNA from a region other than the breakpoint region has been inserted in the breakpoint region, and**
said second probe set being sufficient in length and substantially complementary to **an entire breakpoint region of a second DNA and nucleotides on both sides of the breakpoint region** but less than an entire chromosome such that said second probe set will hybridize **to both sides of the breakpoint region** regardless of whether the second DNA **has been broken in the breakpoint region and either end fused to another DNA.**	said second probe set being sufficient in length and substantially complementary to **a 3' end and a 5' end of a second DNA** but less than an entire chromosome such that said second probe set will hybridize **to both ends of the second DNA** regardless of whether the second DNA **is inserted in the first DNA.**

Claim 1 relates to a probe set which is useful in detecting a particular type of chromosomal rearrangement, called a translocation, in which genetic material is exchanged between two chromosomes. Two probe sets are provided, each of which is substantially complementary to a breakpoint region of a particular DNA. Claim 8 relates to a probe set that is useful in detecting a different type of chromosomal translocation, an insertion, in which a piece of a chromosome is inserted into another chromosome.

However, when the claims are stripped of functional language, it can be seen that the probe sets recited claims 1 and 8 are substantially identical, and where they differ, claim 1 is narrower than – indeed is a species of – claim 8. The first probe set of claim 1 is required to be "sufficient in length and substantially complementary to an entire breakpoint region of a first DNA and nucleotides on both sides of the breakpoint region but less than an entire chromosome." Claim 8 uses exactly the same description of the first probe set in that claim.

The second probe set of claim 1, like the first probe set, is required to be "sufficient in length and substantially complementary to *an entire breakpoint region* of a second DNA and nucleotides on both sides of the breakpoint region but less than an entire chromosome."

(Emphasis added) In contrast, the second probe set of claim 8 is required to be "sufficient in length and substantially complementary to *a 3' end and a 5' end* of a second DNA but less than an entire chromosome." (Emphasis added) It will be readily apparent that "an entire breakpoint region," like any DNA, will necessarily have a 3' and a 5' end, as required by claim 8. However, not all DNA molecules with 3' and 5' ends will represent an entire breakpoint region, as required by claim 1. Thus the second probe set of claim 1 represents a *species* of the genus of claim 8, that would anticipate claim 8 if it were prior art to claim 8. Claim 8 thus represents the same patentable invention as claim 1, and claim 3, and the proposed count.

Claim 9

Claim 9 depends from claim 8, but adds the limitation that the probes are detectably labeled. As noted above, Dietz-Band admits, at col 9, lines 4-32 of the '133 patent, that detectable labels for probes, and methods of labeling probes, are known in the art. As claim 3 (and the proposed Count) also incorporate this limitation, claim 9 is obvious in view of claim 3 and the proposed Count for the same reasons set forth above in connection with claim 8.

Claim 10

Claim 10 is worded similarly to claim 1. A side-by-side comparison of claims 1 and 10 is shown below.

1. A DNA probe set, said probe set comprising a first probe set and a second probe set,	10. A DNA probe set, said probe set comprising a first probe set and a second probe set,
said first probe set being sufficient in length and substantially complementary to **an entire breakpoint region of a first DNA and nucleotides on both sides of the breakpoint region** but less than an entire chromosome such that said first probe set will hybridize to both sides of the breakpoint region regardless of	said first probe set being sufficient in length and substantially complementary to **nucleotides on both sides of the breakpoint region of a first DNA** but less than an entire chromosome such that said first probe set will hybridize to both sides of the breakpoint region regardless of

whether the first DNA has been broken in the breakpoint region and either end fused to another DNA, and	whether a second DNA from a region other than the breakpoint region has been inserted in the breakpoint region, and
said second probe set being sufficient in length and substantially complementary to **an entire breakpoint region of a second DNA and nucleotides on both sides of the breakpoint region** but less than an entire chromosome such that said second probe set will hybridize to both sides of the breakpoint region regardless of whether the second DNA has been broken in the breakpoint region and either end fused to another DNA.	said second probe set being sufficient in length and substantially complementary to **nucleotides on both sides of the breakpoint region of a second DNA** but less than an entire chromosome such that said second probe set will hybridize to both sides of the breakpoint region regardless of whether the second DNA has been broken in the breakpoint region and either end fused to another DNA.

Dietz-Band claim 1 is identical to claim 10 in all but one limitation. Claim 10 requires that the first and second probe sets are complementary to "nucleotides on both sides of the breakpoint region" of the first and second DNA molecules. Claim 1 requires that the first and second probe sets are complementary to "an *entire* breakpoint region . . . and nucleotides on both sides of the breakpoint region."

Any probe set that is complementary to an entire breakpoint region will necessarily be complementary to nucleotides on both sides of the breakpoint region. Consequently, every probe set that meets the limitations of claim 1 will also meet the limitations of claim 10. Thus claim 10 represents a genus of probe sets of which claim 1 is a subset. Claim 1 is thus directed to the same patentable invention as claim 10 because claim 1 would anticipate claim 10 if it were prior art to claim 10. As claim 3 is a species of claim 1, claim 3 is likewise a species of claim 10. Consequently, claim 10 is directed to the same patentable invention as claim 3, and the proposed Count.

Claim 11

Claim 11 depends from claim 10, but adds the limitation that the probes are detectably labeled. As noted above, Dietz-Band admits, at col 9, lines 4-32 of the '133 patent, that detectable labels for probes, and methods of labeling probes, are known in the art. As claim 3

(and the proposed Count) also incorporate this limitation, claim 11 is obvious in view of claim 3 and the proposed Count for the same reasons set forth above in connection with claim 10.

Claim 12

Claim 12 depends from claims 11 (and thus from claim 10), but adds the limitation that "said first DNA is part of the ABL1 gene on chromosome 9" and that "the second DNA is part of the BCR gene on chromosome 22." Dietz-Band admits, at col 1, lines 22-33 of the '133 patent, that breakpoints in the ABL1 gene on chromosome 9 and the BCR gene on chromosome 22 are known in the art to be characteristic of CML. As claim 3 (and the proposed Count) also incorporate these limitations, claim 12 is obvious in view of claim 3 and the proposed Count for the same reasons set forth above in connection with claims 11 and 10.

Claim 14

Claim 14 is directed to a kit comprising a probe set according to claim 10. Kits are conventional in the art. For example, the 1988 Stratagene Catalog. at p. 39, motivates and suggests that the assemblage of materials into kits which may be pre-mixed for the benefits therein cited such as availability and quality testing etc. Kits are also well known in biochemical work with either individual or mixed components ready for use. Thus it would have been obvious to one of ordinary skill in the art at the time of the filing of the '133 patent, in possession of the probe set of claim 10, to assemble the components of that probe set into a kit as suggested by the Stratagene Catalog. As claim 14 is obvious over claim 10, it is likewise obvious over claim 3 and the proposed Count for the reasons discussed above in connection with claim 10.

Claim 15

Claim 15 is directed to a diagnostic kit according to claim 14, comprising at least two containers, each of which contains a reagent comprising a probe set according to claim 10. Claim 15 is obvious over claims 14, 10, and 3, and the proposed Count, for the reasons discussed in connection with claim 14, above.

Claim 16

Claim 16 is directed to a diagnostic kit according to claim 15, wherein the recited reagent contains both the first and second probe set according to claim 10. Claim 16 is obvious over claim 3 and the proposed Count, for the reasons discussed in connection with claims 14 and 15 above.

Claim 17

Claim 17 is directed to a kit comprising a probe set according to claim 8. Kits are conventional in the art. For example, the 1988 Stratagene Catalog at p. 39, motivates and suggests that the assemblage of materials into kits which may be pre-mixed for the benefits therein cited such as availability and quality testing etc. Kits are also well known in biochemical work with either individual or mixed components ready for use. Thus it would have been obvious to one of ordinary skill in the art at the time of the filing of the '133 patent, in possession of the probe set of claim 8, to assemble the components of that probe set into a kit as suggested by the Stratagene Catalog. As claim 17 is obvious over claim 8, it is likewise obvious over claim 3 and the proposed Count, for the reasons discussed above in connection with claim 8.

Claim 18

Claim 18 is directed to a diagnostic kit according to claim 17, comprising at least two containers, each of which contains a reagent comprising a probe set according to claim 8. Claim 18 is obvious over claims 17, 8, and 3, and the proposed Count, for the reasons discussed in connection with claim 17, above.

Claim 19

Claim 19 is directed to a diagnostic kit according to claim 18, wherein the recited reagent contains both the first and second probe set according to claim 8. Claim 19 is obvious over claim 3 and the proposed Count, for the reasons discussed in connection with claims 17 and 18 above.

(4) Presentation of claims corresponding to the proposed Count and explanation why such claims correspond to the proposed Count

Claims 127-143 correspond to the proposed Count. It will be readily appreciated that claim 129 and the proposed Count are identical and therefore, Claim 129 corresponds to the proposed Count. As claims 127-143 are substantially identical to Dietz-Band claims 1-3, 5-12, and 13-19, Applicants submit that claims 127-143 of the instant application correspond to the proposed Count for the reasons set forth in the discussion of the Dietz-Band claims above.

(5) Applying terms of application claims to the disclosure of the application

Attached hereto as Appendix B is a chart providing an element-by-element recitation of the claims of the present application and an indication of exemplary passages in the application where, at the very least, the claims find full support. Applicants emphasize that this support set forth in this chart is only exemplary, and reserve the right to supplement the support for each claim as necessary or desired.

(6) The Requirements of 35 USC 135(b)(1) Are Satisfied.

Section (b)(1) of 35 USC 135 requires that

> A claim which is the same as, or for the same or substantially the same subject matter as, a claim of an issued patent may not be made in any application unless such a claim is made prior to one year from the date on which the patent was granted.

The pending claims in the present application were added by Applicants' Preliminary Amendment filed June 30, 2003. As this is less than one year after the issuance of the '133 patent on July 2, 2002, the terms of 35 USC 135(b)(1) are satisfied.

(7) Conclusion

Applicants respectfully request that examination of the present application be expedited. Applicants also request that an interference be declared:

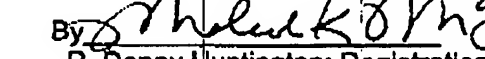
(i) employing the proposed Count set forth in attached Appendix A;

(ii) with claims 1-3, 5-12, and 14-19 of the '133 patent and claims 127-143 of the present application designated as corresponding to the proposed Count; and

(iii) Applicants indicated to be entitled to benefit of the applications listed in footnote 2, above.

Further, upon a determination by the Examiner that an interference should be declared, issuance of a Notice suspending prosecution pending declaration of an interference is respectfully requested. The above actions are respectfully requested.

Respectfully submitted,

By 

R. Danny Huntington; Registration No. 27,903
Malcolm K. McGowan, Ph.D.; Registration No. 39,300

Burns, Doane, Swecker & Mathis
P.O. Box 1404
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Dated: 9 September 2003

APPENDIX A
Proposed Count

A DNA probe set, said probe set comprising a first probe set and a second probe set,

said first probe set being sufficient in length and substantially complementary to an entire breakpoint region of a first DNA and nucleotides on both sides of the breakpoint region but less than an entire chromosome such that said first probe set will hybridize to both sides of the breakpoint region regardless of whether the first DNA has been broken in the breakpoint region and either end fused to another DNA, and

said second probe set being sufficient in length and substantially complementary to an entire breakpoint region of a second DNA and nucleotides on both sides of the breakpoint region but less than an entire chromosome such that said second probe set will hybridize to both ends of the breakpoint region regardless of whether the second has been broken in the breakpoint region and either end fused to another DNA

wherein said probes are detectably labeled, and

wherein said first DNA is part of the ABL1 gene on chromosome 9 and the second DNA is part of the BCR gene on chromosome 22.

APPENDIX B

Exemplary support for the claims in 10/608,092, filed June 30, 2003[3]

CLAIMS - US 6,414,133 (DIETZ-BAND)	PENDING CLAIMS	EXEMPLARY SUPPORT IN SPEC.
1. A DNA probe set, said probe set comprising a first probe set and a second probe set,	127. A DNA probe set, said probe set comprising a first probe set and a second probe set,	"In particular, chromosome specific staining reagents are provided which comprise heterogeneous mixtures of nucleic acid fragments, each fragment having a substantial fraction of its sequences substantially complementary to a portion of the nucleic acid for which specific staining is desired — the target nucleic acid, preferably the target chromosomal material. In general, the nucleic acid fragments are labeled by means as exemplified herein and indicated infra." *p. 18, lines 14-20; ¶ 0071.* "Several different high complexity probes, each labeled by a different method, can be used simultaneously. The binding of different probes can thereby be distinguished, for example, by different colors." *p. 74, lines 15-17; ¶ 0246.*
said first probe set being sufficient in length and substantially complementary to an entire breakpoint region of a first DNA and nucleotides on both sides of the breakpoint region but less than an entire chromosome such that said first probe set will hybridize to both sides of the breakpoint region regardless of whether the first DNA has been broken in the breakpoint region and either end fused to another DNA, and	said first probe set being sufficient in length and substantially complementary to an entire breakpoint region of a first DNA and nucleotides on both sides of the breakpoint region but less than an entire chromosome such that said first probe set will hybridize to both sides of the breakpoint region regardless of whether the first DNA has been broken in the breakpoint region and either end fused to another DNA, and	"The invention provides for nucleic acid probes that reliably stain targeted chromosomal materials in the vicinity of one or more suspected genetic rearrangements. . . . Such nucleic acid probes preferably comprise nucleic acid sequences that are substantially homologous to nucleic acid sequences in chromosomal regions that flank and/or extend partially or fully across breakpoints associated with genetic rearrangements." *p. 19, lines 11-18; ¶ 0073.* "As indicated above, with current

[3] Applicants reserve the right to supplement this table as necessary or desirable.

APPENDIX B

CLAIMS - US 6,414,133 (DIETZ-BAND)	PENDING CLAIMS	EXEMPLARY SUPPORT IN SPEC.
		hybridization techniques it is possible to obtain a reliable, easily detectable signal with a probe of about 40 to about 100 kb (e.g. the probe insert capacity of one or a few cosmids) targeted to a compact point in the genome. Thus, for example, a complexity in the range of approximately 100 kb now permits hybridization to both sides of a tumor-specific translocation. The portion of the probe targeted to one side of the breakpoint can be labeled differently from that targeted to the other side of the breakpoint so that the two sides can be differentiated with different colors, for example." p. 38, lines 8-16; ¶ 0141. "32. High complexity nucleic acid probes for the detection of genetic rearrangements. 111. Nucleic acid probes, according to claim 32, comprising nucleic acid sequences that ~~are substantially homologous to nucleic acid~~ sequences in chromosomal regions that flank and/or extend partially or fully across breakpoints associated with cytogenetically similar but genetically different diseases." Original claims 32 and 111 See also, Fig. 11, and description below

APPENDIX B

CLAIMS - US 6,414,133 (DIETZ-BAND)	PENDING CLAIMS	EXEMPLARY SUPPORT IN SPEC.
said second probe set being sufficient in length and substantially complementary to an entire breakpoint region of a second DNA and nucleotides on both sides of the breakpoint region but less than an entire chromosome such that said second probe set will hybridize to both sides of the breakpoint region regardless of whether the second DNA has been broken in the breakpoint region and either end fused to another DNA.	said second probe set being sufficient in length and substantially complementary to an entire breakpoint region of a second DNA and nucleotides on both sides of the breakpoint region but less than an entire chromosome such that said second probe set will hybridize to both sides of the breakpoint region regardless of whether the second DNA has been broken in the breakpoint region and either end fused to another DNA.	see above; also "Figure 11 illustrates some exemplary probe strategies for detection of structural aberrations. . . . Section a) represents the use of a probe which stains a whole chromosome . . . . Section b) represents the reduction of the stained region of the chromosome shown in a) to that in the vicinity of a breakpoint . . . Section c) represents the use of a probe which binds to sequences which come together as a result of the rearrangement and allows for the detection in metaphase and interphase cells. In this case the different sequences are stained with different 'colors.' Such a staining pattern is that used in the examples of Section VIII of this application . . .. Section d) represents an extension of c) by including staining of both sides of both breakpoints involved in the rearrangement. Different 'colors' are used as indicated. The additional information supplied by the more complex staining pattern may assist with interpretation of the nuclei." p. 31, line 1 - p. 32, line 19; ¶ 0122-0127.

APPENDIX B

CLAIMS - US 6,414,133 (DIETZ-BAND)	PENDING CLAIMS	EXEMPLARY SUPPORT IN SPEC.
2. The probe set of claim 1, wherein said probes are detectably labeled.	128. The probe set of claim 127, wherein said probes are detectably labeled.	"Section III *infra* describes methods of rendering the probe visible. Since multiple compatible methods of probe visualization are available, the binding patterns of different components of the probe can be distinguished — for example, by color. Thus, this invention is capable of producing any desired staining pattern on the chromosomes visualized with one or more colors (a multi-color staining pattern) and/or other indicator methods." *p. 36, lines 17-23; ¶ 0137.* See also, *Section III. "Labeling the Nucleic Acid Fragments of the Heterogeneous Mixture," at pp 72-74; ¶. 0241-0246.*

APPENDIX B

CLAIMS - US 6,414,133 (DIETZ-BAND)	PENDING CLAIMS	EXEMPLARY SUPPORT IN SPEC.
3. The probe set of claim 2, wherein said first DNA is part of the ABL1 gene on chromosome 9 and the second DNA is part of the BCR gene on chromosome 22.	129. The probe set of claim 128, wherein said first DNA is part of the ABL1 gene on chromosome 9 and the second DNA is part of the BCR gene on chromosome 22.	"Specifically herein exemplified are chromosome specific reagents and methods to detect genetic rearrangements . . . that produce the BCR-ABL fusion which is diagnostic for chronic myelogenous leukemia (CML). Such chromosome specific reagents for the diagnosis of CML contain nucleic acid sequences which are substantially homologous to chromosomal sequences in the vicinity of the translocation breakpoint regions of chromosomal regions 9q34 and 22q11 associated with CML. Those reagents produce a staining pattern which is distinctively altered when the BCR-ABL fusion characteristic of CML occurs. Figure 11 graphically demonstrates a variety of staining patterns which, along with other potential staining patters, are altered in the presence of a genetic rearrangement, such as, the BCR-ABL fusion." *p. 19, line 22 - p. 20, line 8; ¶ 0075-0076.*
		"Figure 8 illustrates the locations of probes to the CML breakpoint and corresponding pattern of staining in both normal and CML metaphase and interphase nuclei. The left side shows schematic representations of the BCR gene on chromosome 22, the ABL gene of chromosome 9, and the BCR-ABL fusion gene on the Philadelphia chromosome. Also shown are the locations of CML breakpoints and their relation to the probes (32)." *p. 29, line 24 - p. 30, line 6; ¶ 118-119.*

APPENDIX B

CLAIMS - US 6,414,133 (DIETZ-BAND)	PENDING CLAIMS	EXEMPLARY SUPPORT IN SPEC.
5. A diagnostic kit for detecting a structural abnormality caused by chromosomal breakage and rearrangement containing a reagent comprising at least one probe set of the probe set according to claim 1, and a container containing said reagent.	130. A diagnostic kit for detecting a structural abnormality caused by chromosomal breakage and rearrangement containing a reagent comprising at least one probe set of the probe set according to claim 127, and a container containing said reagent.	"This invention still further provides for test kits comprising appropriate nucleic acid probes for use in tumor cytogenetics, in the detection of disease related loci, in the analysis of structural abnormalities, for example translocations, among other genetic rearrangements, and for biological dosimetry." *p. 25, lines 8-12; ¶0095.*
6. A diagnostic kit according to claim 5 further comprising at least two containers, wherein a first container contains a reagent comprising said first probe set and a second container contains a reagent comprising said second probe set.	131. A diagnostic kit according to claim 130 further comprising at least two containers, wherein a first container contains a reagent comprising said first probe set and a second container contains a reagent comprising said second probe set.	*See claim 130, above*
7. A diagnostic kit according to claim 6 wherein said reagent comprises said first and said second probe set.	132. A diagnostic kit according to claim 131 wherein said reagent comprises said first and said second probe set.	*See claim 131, above*
8. A DNA ~~probe set, said probe set~~ comprising a first probe set and a second probe set,	133. A DNA probe set, said probe set comprising a first probe set and a second probe set,	"In particular, chromosome specific staining reagents are provided which comprise heterogeneous mixtures of nucleic acid fragments, each fragment having a substantial fraction of its sequences substantially complementary to a portion of the nucleic acid for which specific staining is desired — the target nucleic acid, preferably the target chromosomal material. In general, the nucleic acid fragments are labeled by means as exemplified herein and indicated infra." p. 18, lines 14-20
said first probe set being sufficient in length and substantially complementary to an entire breakpoint region of a first DNA and nucleotides on both sides of the breakpoint region but less than an entire chromosome such that said first probe set will hybridize to	said first probe set being sufficient in length and substantially complementary to an entire breakpoint region of a first DNA and nucleotides on both sides of the breakpoint region but less than an entire chromosome such that said first probe set will hybridize to	"As indicated above, with current hybridization techniques it is possible to obtain a reliable, easily detectable signal with a probe of about 40 to about 100 kb (eg. the probe insert capacity of one or a few cosmids) targeted to a compact point in the

APPENDIX B

CLAIMS - US 6,414,133 (DIETZ-BAND)	PENDING CLAIMS	EXEMPLARY SUPPORT IN SPEC.
both sides of the breakpoint region regardless of whether a second DNA from a region other than the breakpoint region has been inserted in the breakpoint region, and	both sides of the breakpoint region regardless of whether a second DNA from a region other than the breakpoint region has been inserted in the breakpoint region, and	genome. Thus, for example, a complexity in the range of approximately 100 kb now permits hybridization to both sides of a tumor-specific translocation. The portion of the probe targeted to one side of the breakpoint can be labeled differently from that targeted to the other side of the breakpoint so that the two sides can be differentiated with different colors, for example." *p. 38, lines 8-16; ¶ 0141.* "32. High complexity nucleic acid probes for the detection of genetic rearrangements. 111. Nucleic acid probes, according to claim 32, comprising nucleic acid sequences that are substantially homologous to nucleic acid sequences in chromosomal regions that flank and/or extend partially or fully across breakpoints associated with cytogenetically similar but genetically different diseases." Original claims 32 and 111 ~~See also, Fig. 11, and description below~~
said second probe set being sufficient in length and substantially complementary to a 3' end and a 5' end of a second DNA but less than an entire chromosome such that said second probe set will hybridize to both ends of the second DNA regardless of whether the second DNA is inserted in the first DNA.	said second probe set being sufficient in length and substantially complementary to a 3' end and a 5' end of a second DNA but less than an entire chromosome such that said second probe set will hybridize to both ends of the second DNA regardless of whether the second DNA is inserted in the first DNA.	see above; also "The invention concerns chromosome specific reagents and methods of staining targeted chromosomal material that is in the vicinity of a suspected genetic rearrangement. Such genetic rearrangement include but are not limited to . . . insertions" *p. 19, lines 3-7; ¶0072.* "Figure 9 shows a fluorescence in-situ hybridization (FISH) in metaphase spreads and interphase nuclei . . . Panel D shows that abl staining is interstitial on the derivative 22

APPENDIX B

CLAIMS - US 6,414,133 (DIETZ-BAND)	PENDING CLAIMS	EXEMPLARY SUPPORT IN SPEC.
		chromosome arising from an insertional event in a case of CMP with 46XY INS (22:9) (q11;q34)." *p. 30, lines 7-15; ¶ 0121.* "Figure 11 illustrates some exemplary probe strategies for detection of structural aberrations . . . Section d) represents an extension of c) by including staining of both sides of both breakpoints involved in the rearrangement. Different 'colors' are used as indicated. The additional information supplied by the more complex staining pattern may assist with interpretation of the nuclei. It might also permit recognition of an apparent insertional event as discussed herein." *p. 31, line 1 – p. 32, line 21; ¶ 0122-0127.* "One case (CML-6) was suspected by classical cytogenetics to have an insertion of chromosomal material at 22q11. Dual color hybridization to metaphase spreads from this case showed the red-green pair to be centrally located in a small chromosome (Figure 9D). That result is consistent with the formation of the BCR-ABL fusion gene by an insertion." *p. 122, lines 6-10; ¶ 0354.*

APPENDIX B

CLAIMS - US 6,414,133 (DIETZ-BAND)	PENDING CLAIMS	EXEMPLARY SUPPORT IN SPEC.
9. The probe set of claim 8, wherein said probes are detectably labeled.	134. The probe set of claim 133, wherein said probes are detectably labeled.	"Section III *infra* describes methods of rendering the probe visible. Since multiple compatible methods of probe visualization are available, the binding patterns of different components of the probe can be distinguished — for example, by color. Thus, this invention is capable of producing any desired staining pattern on the chromosomes visualized with one or more colors (a multi-color staining pattern) and/or other indicator methods." *p. 36, lines 17-23, ¶ 0137.* See also, *Section III. "Labeling the Nucleic Acid Fragments of the Heterogeneous Mixture," at pp 72-74; ¶ 0241-0246.*
10. A DNA probe set, said probe set comprising a first probe set and a second probe set,	135. A DNA probe set, said probe set comprising a first probe set and a second probe set,	"In particular, chromosome specific staining reagents are provided which comprise heterogeneous mixtures of nucleic acid fragments, each fragment having a substantial fraction of its sequences substantially complementary to a portion of the nucleic acid for which specific staining is desired — the target nucleic acid, preferably the target chromosomal material. In general, the nucleic acid fragments are labeled by means as exemplified herein and indicated infra." *p. 18, lines 14-20; ¶ 0071.*
said first probe set being sufficient in length and substantially complementary to nucleotides on both sides of the breakpoint region of a first DNA but less than an entire chromosome such that said first probe set will hybridize to both sides of the breakpoint region regardless of whether the first DNA has been broken in the breakpoint region and either end fused to another DNA, and	said first probe set being sufficient in length and substantially complementary to nucleotides on both sides of the breakpoint region of a first DNA but less than an entire chromosome such that said first probe set will hybridize to both sides of the breakpoint region regardless of whether the first DNA has been broken in the breakpoint region and either end fused to another DNA, and	"As indicated above, with current hybridization techniques it is possible to obtain a reliable, easily detectable signal with a probe of about 40 to about 100 kb (eg. the probe insert capacity of one or a few cosmids) targeted to a compact point in the genome. Thus, for example, a complexity in the range of approximately 100 kb now permits hybridization to both sides of a tumor-

APPENDIX B

CLAIMS - US 6,414,133 (DIETZ-BAND)	PENDING CLAIMS	EXEMPLARY SUPPORT IN SPEC.
		specific translocation. The portion of the probe targeted to one side of the breakpoint can be labeled differently from that targeted to the other side of the breakpoint so that the two sides can be differentiated with different colors, for example." *p. 38, lines 8-16; ¶ 0141.* "32. High complexity nucleic acid probes for the detection of genetic rearrangements. 111. Nucleic acid probes, according to claim 32, comprising nucleic acid sequences that are substantially homologous to nucleic acid sequences in chromosomal regions that flank and/or extend partially or fully across breakpoints associated with cytogenetically similar but genetically different diseases." Original claims 32 and 111 See also, Fig. 11, and description below
said second probe set being sufficient in length and substantially complementary to nucleotides on both sides of the breakpoint region of a second DNA but less than an entire chromosome such that said second probe set will hybridize to both sides of the breakpoint region regardless of whether the second DNA has been broken in the breakpoint region and either end fused to another DNA.	said second probe set being sufficient in length and substantially complementary to nucleotides on both sides of the breakpoint region of a second DNA but less than an entire chromosome such that said second probe set will hybridize to both sides of the breakpoint region regardless of whether the second DNA has been broken in the breakpoint region and either end fused to another DNA.	see above; also "Figure 11 illustrates some exemplary probe strategies for detection of structural aberrations. . . . Section a) represents the use of a probe which stains a whole chromosome. . . . Section b) represents the reduction of the stained region of the chromosome shown in a) to that in the vicinity of a breakpoint. . . Section c) represents the use of a probe which binds to sequences which come together as a result of the rearrangement and allows for the detection in metaphase and interphase cells. In this case the different sequences are stained with different 'colors.' Such a staining pattern is

APPENDIX B

CLAIMS - US 6,414,133 (DIETZ-BAND)	PENDING CLAIMS	EXEMPLARY SUPPORT IN SPEC.
		that used in the examples of Section VIII of this application. . . . Section d) represents an extension of c) by including staining of both sides of both breakpoints involved in the rearrangement. Different 'colors' are used as indicated. The additional information supplied by the more complex staining pattern may assist with interpretation of the nuclei." *p. 31, line 1 - p. 32, line 19; ¶ 0122-0127.*
11. The probe set of claim 10, wherein said probes are detectably labeled.	136. The probe set of claim 135, wherein said probes are detectably labeled.	"Section III *infra* describes methods of rendering the probe visible. Since multiple compatible methods of probe visualization are available, the binding patterns of different components of the probe can be distinguished — for example, by color. Thus, this invention is capable of producing any desired staining pattern on the chromosomes visualized with one or more colors (a multi-color staining pattern) and/or other indicator methods." *p. 36, lines 17-23; ¶ 0137.*
12. The probe set of claim 11, wherein said first DNA is part of the ABL1 gene on chromosome 9 and the second DNA is part of the BCR gene on chromosome 22.	137. The probe set of claim 136, wherein said first DNA is part of the ABL1 gene on chromosome 9 and the second DNA is part of the BCR gene on chromosome 22.	"Specifically herein exemplified are chromosome specific reagents and methods to detect genetic rearrangements . . . that produce the BCR-ABL fusion which is diagnostic for chronic myelogenous leukemia (CML). Such chromosome specific reagents for the diagnosis of CML contain nucleic acid sequences which are substantially homologous to chromosomal sequences in the vicinity of the translocation breakpoint regions of chromosomal regions 9q34 and 22q11 associated with CML. Those reagents produce a staining pattern which is distinctively altered when the

APPENDIX B

CLAIMS - US 6,414,133 (DIETZ-BAND)	PENDING CLAIMS	EXEMPLARY SUPPORT IN SPEC.
		BCR-ABL fusion characteristic of CML occurs. Figure 11 graphically demonstrates a variety of staining patterns which, along with other potential staining patters, are altered in the presence of a genetic rearrangement, such as, the BCR-ABL fusion." *p. 19, line 22 - p. 20, line 8; ¶ 0075-0076.*
14. A diagnostic kit for detecting a structural abnormality caused by chromosomal breakage and rearrangement containing a reagent comprising at least one probe set of the probe set according to claim 10, and a container containing said reagent.	138. A diagnostic kit for detecting a structural abnormality caused by chromosomal breakage and rearrangement containing a reagent comprising at least one probe set of the probe set according to claim 135, and a container containing said reagent.	"This invention still further provides for test kits comprising appropriate nucleic acid probes for use in tumor cytogenetics, in the detection of disease related loci, in the analysis of structural abnormalities, for example translocations, among other genetic rearrangements, and for biological dosimetry." *p. 25, lines 8-12; ¶ 0095.*
15. A diagnostic kit according to claim 14 further comprising at least two containers, wherein a first container contains a reagent comprising said first probe set and a second container contains a reagent comprising said second probe set.	139. A diagnostic kit according to claim 138 further comprising at least two containers, wherein a first container contains a reagent comprising said first probe set and a second container contains a reagent comprising said second probe set.	*see claim 138, above*
16. A diagnostic kit according to claim 15 wherein said reagent comprises said first and said second probe sets.	140. A diagnostic kit according to claim 139 wherein said reagent comprises said first and said second probe sets.	*see claim 139, above*
17. A diagnostic kit for detecting a structural abnormality caused by chromosomal breakage and rearrangement containing a reagent comprising at least one probe set of the probe set according to claim 8, and a container containing said reagent.	141. A diagnostic kit for detecting a structural abnormality caused by chromosomal breakage and rearrangement containing a reagent comprising at least one probe set of the probe set according to claim 133, and a container containing said reagent.	"This invention still further provides for test kits comprising appropriate nucleic acid probes for use in tumor cytogenetics, in the detection of disease related loci, in the analysis of structural abnormalities, for example translocations, among other genetic rearrangements, and for biological dosimetry." *p. 25, lines 8-12; ¶ 0095.*
18. A diagnostic kit according to claim 17 further comprising at least two containers,	142. A diagnostic kit according to claim 141 further comprising at least two containers,	*see claim 141, above*

APPENDIX B

CLAIMS - US 6,414,133 (DIETZ-BAND)	PENDING CLAIMS	EXEMPLARY SUPPORT IN SPEC.
wherein a first container contains a reagent comprising said first probe set and a second container contains a reagent comprising said second probe set.	wherein a first container contains a reagent comprising said first probe set and a second container contains a reagent comprising said second probe set.	
19. A diagnostic kit according to claim 18 wherein said reagent comprises said first and said second probe sets.	143. A diagnostic kit according to claim 142 wherein said reagent comprises said first and said second probe sets.	*see claim 142, above*

Application Serial No. 10/608,092
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